UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/795,933	03/08/2004	Jan Zavada	D-0021.2-2	2689

24988 7590 06/12/2007

LEONA L. LAUDER
235 MONTGOMERY STREET, SUITE 1026
SAN FRANCISCO, CA 94104-0332

EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
06/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/795,933	ZAVADA ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-35 and 39-55* is/are pending in the application.

4a) Of the above claim(s) *41-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-35, 39-40, 53-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on May 1, 2007.

Currently, claims 31-35, 39-40, and 53-55 are under examined on the merits.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Terminal Disclaimers

The terminal disclaimer filed on May 1, 2007 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US 6,774,117 B1 has been reviewed and is accepted. The terminal disclaimer has been recorded. This terminal disclaimer pertains to claims 39-40.

Note that applicant has previously filed a terminal disclaimer on September 13, 2006 in response to double patenting rejections for claims 31-35 and 53-55, disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US 5,387,676.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

New Rejections

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31-35, 39-40, and 53-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims are drawn to MN antisense constructs comprising a nucleic acid sequence from which an MN antisense oligonucleotide is transcribable and the methods of inhibiting MN expression comprising administering the MN antisense constructs.

The specification, as originally filed, discloses antisense oligodeoxynucleotides that are complementary to MN mRNA sequence, wherein the antisense oligodeoxynucleotides are 19-mer or 29-mer (Example 10; Figure 3). It also discloses methods wherein naked antisense oligonucleotides (i.e., without being expressed by an expression vector) are added to the cell culture media. See Example 10. With regard to an expression vector, the specification discloses

an antisense MN cDNA/promoter construct (page 65), wherein the full-length MN cDNA sequence comprising 1519 nucleotides in length is placed in an antisense orientation and the promoter is an MN promoter (page 40; Figure 15). Nevertheless, the specification is completely silent about a vector that is capable of transcribing an antisense oligonucleotide in a human cell with a resultant decrease in the MN expression in the cell or claimed therapeutic effect of treating a neoplastic disease. Further, the specification does not describe SEQ ID NO:7 as a potential antisense oligonucleotide that decreases MN expression as claimed in claim 55; rather, it describes SEQ ID NO:7 only as a reverse primer sequence that is used in a RACE system for full-length MN cDNA cloning experimentation (page 39). Nowhere in the specification is there a disclosure which indicates that the inventors contemplated SEQ ID NO:7 as an antisense oligonucleotide that decreases MN expression in a human cell as claimed in the instant case. Accordingly, the instantly claimed subject matter introduces a new matter that was not originally disclosed in the application as filed, and hence, it is concluded that the claimed subject matter was not described in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed.

Claims 31-35, 39-40, and 53-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The

Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'." (Wands, 8 USPQ2d 1404). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The claims are drawn to MN antisense constructs comprising a nucleic acid sequence from which an MN antisense oligonucleotide is transcribable and the methods of inhibiting MN expression comprising administering the MN antisense constructs.

The specification teaches that the MN antisense oligonucleotide is preferably between 19 to 29 nucleotides in length. See page 94.

Since Zamecnik and Stephenson first published their reports on antisense oligonucleotides that inhibit the targeted RNA in 1978 (see *PNAS* references cited in the PTO form 892), the effective delivery methods which utilize an expression vector and a promoter for expressing and producing short antisense oligonucleotides in mammalian cells were neither routinely practiced in the art nor practically conceived of in the art until the 1994 publication by Noonberg et al. (*Nucleic Acids Research,* 1994, 22:2830-2836), which teaches that short inhibitory oligonucleotide sequences such as antisense oligonucleotides, ribozymes, and triplex

are expressed by the U6 promoter within the U6 vector. Combined with the fact that the specification is silent about the therapeutic effect of treating a neoplastic disease in a human comprising administering a vector transcribing an antisense oligonucleotide, the lack of sufficient teachings of the prior art to the present application such that short oligonucleotides can be transcribed from an expression vector in cells corroborates low level of predictability encompassed in the vector transcribing a short antisense oligonucleotide in human cells, which is also claimed to be used as a therapeutic agent for neoplastic disease treatment.

To further substantiate the unpredictability entailed in the vector that expresses a short antisense oligonucleotide in human cells either *in vitro* or *in vivo* as of the earliest filing date sought in the instant case (that is the year of 1992), none of the references incorporated in the specification teaches, let alone insinuates, the feasibility or conception of cloning short antisense oligonucleotides into a vector. See pages 92-93 for the references incorporated by the inventors.

Furthermore, the declaration under 37 CFR 1.132 filed on January 4, 2007 addresses a plasmid containing antisense MN "cDNA" or naked MN antisense oligonucleotides; however, nowhere in the 8-page declaration is there a statement acknowledging that a plasmid or vector can successfully express MN antisense oligonucleotides in cells and confer therapeutic effects. In addition, the Mirabelli et al. reference attached to the declaration does not teach anything that is remotely close to a vector expressing a short antisense oligonucleotide in cells with a resultant pharmacologic activities of the antisense oligonucleotide.

Also note that the specification does not teach that the naked MN antisense oligonucleotide interacts with MN gene at the DNA level as claimed in claim 35, although it shows the MN antisense oligonucleotide blocks MN transcript at the mRNA level.

In light of the above reasons and the totality of the factors listed above, it is reasonably believed that it would have necessitated an undue experimentation to construct a vector that is capable of expressing a short (19-29 mer) antisense oligonucleotide in a human cell or to use such vector to treat a neoplastic disease in a human, especially because the state of the prior art, the level of one of ordinary skill in the art, the amount of direction provided by the inventor, and the level of unpredictability in the art were substantially nadir as of the year of 1992. Accordingly, the instant specification has failed to satisfy the enablement requirement set forth in 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 53 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 53 recites the limitation "said promoter" in line 2. There is insufficient antecedent basis for this limitation in the claim. Note that claim 31 does not recite the term “promoter”.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/J. E. Angell/
Primary Examiner
AU 1635